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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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BRUNOVSKIS,P	
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DATE MAILED: 02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/513,997	Harrington et al.
Examiner	**Group Art Unit**
Peter Brunovskis	1632

☒ Responsive to communication(s) filed on *Dec 1, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *58-105* is/are pending in the applicat

Of the above, claim(s) *58-80, 82, 89-91, 93-99, 104, and 105* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *81, 83-88, 92, and 100-103* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2 and 4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

Applicant's election without traverse of Group V, claims 81, 83-88, 92, and 100-103 in Paper No. 7, filed 12/01/00 is acknowledged.

Claims 58-80, 82, 89-91, 93-99, and 104-105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Information Disclosure Statement

The Information Disclosure Statement, filed 2/26/00 (Paper No. 2), states that "[a]ll items are attached except those that were supplied in parent Application No. 09/276,820 filed March 26, 1999". The statement correctly states that "[s]ince the benefit of this application was claimed under 35 U.S.C. 120, no copies need to be furnished in accordance with 37 C.F.R. 1.98(d)". However, 37 C.F.R. 1.98(d) stipulates that copies are need not be furnished *"provided that the prior application is properly identified in the statement*" (emphasis added). In the instant case, most of the references were not found to be enclosed in the '820' application as stated. Consequently, it is sincerely requested that Applicants provide copies of AC2, AN2, and AO2 since these were not found and could not be considered.

Further, with regard to reference AO2 (FR 2 707 091), the information disclosure statement filed 2/26/00 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language (i.e. AO2).

Claim Objections

Claims 83, 88, 92, and 100-102 (and dependent claims) are objected to because of the following informalities: The objected claims are recited as depending on non-elected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 81, 83-88, 92, and 100-103 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 81 and 100 (and dependent claims) are indefinite in their recitation of "endogenous gene" or "endogenous cellular gene" since it is not clear what the nature of the endogenous gene is: an endogenous gene in its native chromosomal locus or a gene (e.g. transgene) that is endogenous to an animal. For example, a mouse erythropoietin transgene expressed from a vector in mouse cells could be considered "endogenous" to mice. The Academic Press Online Dictionary of Science and Technology defines "endogenous" as "*originating*, developing, or growing from within" (emphasis added).

Claim 81 (and dependent claims) is indefinite in its recitation of "over-expressing", and "overexpression", since it is unclear how these terms are defined or what context applies to these limitations--whether, e.g. said over-expression (levels) applies to expression levels relative to endogenous genes (prior to activation) and/or relative to other cells expressing the same *or different* gene products (or expression products).

Claims 81 (and dependent claims) is indefinite in its recitation of "expression product", and "portion thereof", since it is not clear how these terms are defined in the context of an "endogenous gene"--whether the resultant products refer to mRNAs, proteins, or some undefined "portion[s] thereof", for example.

Claim 81 (and dependent claims) is indefinite in its recitation of "screening said cell" since it is unclear how screening applies to "a cell" (singular) and since "over-express[ion] [of] an endogenous gene or portion thereof in *said cell* [singular form; emphasis added]" would not

appear to require any subsequent "screening" steps (since it is already established, e.g. step (c) to be over-expressing said endogenous gene)..

Claim 81 (and dependent claims) recites the limitation "said isolated and cloned cell" in step (e). There is insufficient antecedent basis for this limitation in the claim.

Claim 81 (and dependent claims) is incomplete since the method steps do not clearly relate back to "[a] method for over-expressing an endogenous gene in a cell *in vivo*" since the method steps do not list any steps that actually recite over-express[ion] of an endogenous gene *in vivo*, but rather the "over-express[ion] [of] an endogenous gene or a portion thereof in *said cell*"(presumably *in vitro*, in step (c), although this is not clear) and the screening and culturing of isolated or cloned cells (in steps (d) and (e)). Also, it is not clear how what *"in vivo"* means in the context of the preamble--the method for over-expressing an endogenous gene *in a cell* does not change upon introduction of into an animal. Moreover, it is unclear whether, the method steps initially involve introduction of vector into a cell in vitro or systemic introduction in vivo followed by screening and (re)introduction of the cloned cell(s) via *ex vivo* gene transfer.

Claim 81 (and dependent claims) are indefinite in their recitation of method steps (b) and (e) because the limitations recited do not appear to represent active process steps subject to the control of the artisan. Inasmuch as these steps do not appear to be under the control of the artisan, it is not clear what is meant by these steps in the context of the recited method. For example, it is unclear what is meant by "integrating said construct into the genome...by non-homologous recombination" with- (i.e. cl.88) or without a requirement for artificially-introduced

DNA breaks (e.g. cl. 81, 83-87), since the recited methods are not accompanied by specific active process steps or limitations specifically directed to the process of non-homologous integration, nor are the method steps specifically directing "integrat[ion]" or "over-expressi[on]" under the uncontrolled conditions recited (see also 35 U.S.C. 102 rejection over Treco, as evidenced by Capecchi below).

Claim 92 recites the limitation "said vector construct" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 81, 83-88, 92, and 100-103 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In determining whether the specification provides an enabling disclosure for the claimed subject matter of claims 81, 83-88, 92, and 100-103, the factors for consideration are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine

screening. However, experimentation needed to practice the invention must not be undue experimentation....Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Factors that can be used in evaluating undue experimentation include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Claims 81-88 are drawn to methods for over-expressing endogenous genes *in vivo*. Upon evaluation of the specification in the instant application and in the parent applications, the only specific utility for the claimed method described in parent application 08/941,223 is in the context of *cells* to be used in vivo to provide that gene product in the intact animal (e.g. p. 8, lines 14-15; p. 16, lines 14-15; p. 48, lines 7-9) or for use of "[c]ells produced by this method...[to] be used...in vivo (e.g. for use in cell therapy)" (p. 29). The instant application essentially provides no further description or guidance concerning in vivo use of the claimed method beyond the limited descriptions alluded to in the '223' application (see e.g. p. 8, top paragraph; p. 10, lines 26-27; p. 36, lines 1-2, 18-19; p. 37, lines 3-4; p. 51, line 21 through p. 52, line 4; p. 52, lines 15-25; p. 54, lines 26-27; p. 71, lines 27-30). The specification fails to provide any written description or guidance for providing cells expressing endogenous gene products of the claimed method to an intact animal (e.g. or "desired amounts" thereto), except for reference to "use in cell therapy" as

described on p. 29, lines 24-25 and p. 54, lines 26-27 of the '223' and instant applications, respectively. Therefore, the only specific and substantial utility that could be gleaned from the instant disclosure is for use of the method in cell therapy which is interpreted to mean ex vivo gene therapy.

At the time the invention was made the technology for the successful use of *ex vivo* gene therapy was not routinely achieved (see for example, Kay et al., Proc. Natl. Acad. Sci. USA, 94:12744-12746, 11/97, p. 12746; Anderson, Nature, 392:25-30, 4/98, p. 25, top right column). Furthermore, at the time the invention was made, attempts at *ex vivo* gene therapy were essentially focused on transfer of transduced hematopoietic stem cells. While lethally irradiated mice can be reconstituted with retroviral vector transduced syngeneic bone marrow, such that the cells can provide genetically marked progeny persisting in blood and bone marrow over extended time periods, hematopoietic stem cells from large animals are much more refractory to gene transfer, cell engraftment, and sustained long-term expression coincident with HSC repopulation and expansion (Chu et al., J. Mol. Med., 76:184-192, 1998). Kay reported that the frequency of retrovirally transduced stem cells after transplantation in a human subject is only 0.001% of the endogenous stem cells, too low to result in detectable, stable engraftment (p. 12746, left column). A retroviral transduction efficiency leading to 0.01%-5% provirus positive circulating cells is too low to expect clinical improvement for the majority of human diseases associated with the hematopoietic system (Havenga et al., Stem Cells, 15:162-179, 1997). Since most HSCs are quiescent and do not support most types of retroviral gene transfer, many recent attempts have

employed (in addition to CD34+CD38- cell selection) the use of growth factors or cocultivation with genetically engineered stromal cell lines or preformed stromal layers (Chu et al., p. 187, top left paragraph). However, while the above approaches have demonstrated reasonably high levels of gene transfer into hematopoietic progenitors, gene transfer into HSCs assessed by *in vivo* reconstitution experiments in cats, dogs, and monkeys have failed to demonstrate clinically relevant levels of HSC gene transfer (p. 187, bottom left paragraph). In the majority of these latter studies fewer than 2% of hematopoietic cells and progenitors in the marrow and blood contained proviral sequences by 1 year posttransplant despite the use of *in vivo* cytoablation regimens, coculture with retroviral producer cell lines or engineered stromal cell lines, inclusion of growth factors during retroviral transduction, and/or the enrichment of hematopoietic progenitors and HSCs. Taken together, these results led Chu et al. to conclude that "currently available HSC gene-transfer protocols do not reliably transfer genes into HSCs with long-term repopulating capacity" (p. 189, last paragraph). Havenga lent a similar assessment in concluding that "for gene therapy to become a clinically relevant treatment, several problems have to be overcome...includ[ing] the identification of human PHSCs and the golden mixture of factors allowing *ex vivo* PHSC cycling and transduction without losing grafting potential" (p. 174, last paragraph).

The physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher,* 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that the scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Given the lack of success in the *ex vivo* gene therapy art (i.e cell therapy), and the unpredictability of the physiological art, the need for clear and specific guidance, including working examples is underscored. However, no such guidance has been provided, beyond *the mere assertion of the use of the cells from the claimed method "for use in cell therapy"*. No further guidance is provided. For example, there is no guidance concerning requisite recombinant cell compositions, dosages, methodology for *in vivo* recombinant cell administration (and/or engraftment) in animals, nor guidance concerning selection of animals or patients in need of such compositions.

It is further noted that the instant disclosure does not provide any evidence of a specific, substantial, credible, or well-established utility for non-therapeutic *in vivo* administration of the recombinant cells of the claimed invention. Furthermore, any asserted use of the recited compositions or methods of the claimed invention for research purposes would raise issues of whether the utilities require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See , e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility".

Considering the unpredictable and undeveloped state of the art as described above, it would likely require considerable experimentation to appropriately develop the claimed invention for *in vivo* cell therapy or *in vivo* cell transfer as recited in claims 81, 83-88, 92, and 100-103. This is particularly true given the state of the art, the nature of the invention, the unpredictability of the art, the scarcity of guidance and working examples in the specification, and the amount of experimentation necessary.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 81, 83, 86, 87, 92, and 100-102 are rejected under 35 U.S.C. 102(e) as being anticipated by Sands et al. (U.S. 6,136,566, filed 10/4/96) and as further evidenced by Vasallo et al. (Bioch. Biophys. Res. Commun., 270(3):1036-1040, 4/00).

Sands discloses a method for producing an expression product of an endogenous cellular gene in vivo, comprising introducing a vector comprising a transcriptional regulatory sequence in

an embryonic stem cell; integrating said vector into the genome of said cell by non-homologous recombination; overexpressing an endogenous gene or a portion thereof in said cell by upregulation of said gene by said transcriptional regulatory sequence; screening said cell for over-expression of said endogenous gene; and introducing said isolated and cloned embryonic stem cell into an animal under conditions favoring the creation of transgenic animals overexpressing said endogenous gene by said cell in vivo (see e.g. col. 11, lines 12-30; col. 15, line 64 through col. 18, line 11). Sands further discloses vectors wherein the transcriptional regulatory sequence is a non-viral promoter (e.g. PGK promoter; Fig. 1 and col. 16, line 3) and a method of using said vector wherein said vector construct is linear (e.g. col. 16, line 10). Sands further discloses that "[s]ince the coverage of the mutagenesis is preferably the entire set of genes in the genome, the resulting Library sequence database contains sequence from essentially every gene in the cell" (col. 4, lines 24-28); consequently, Sands anticipates the method of claim 100 drawn to the method of claim 81 wherein said endogenous gene encodes a transmembrane protein. Vassallo discloses that the PGK promoter can be induced by paraquat.

Claims 81, 83-88, 92, and 100-103 are rejected under 35 U.S.C. 102(e) or 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Treco et al. (US 5,641,670, filed 5/13/94) as evidenced by Capecchi (Sci. Amer., 270(3):52-59, 3/94).

Treco discloses a method for over-expressing an endogenous gene in a cell in vivo comprising ex vivo introduction into humans of cells transformed with a vector comprising a

transcriptional regulatory sequence for integration into a cellular genome and activation of endogenous cellular genes (e.g. col. 7, lines 1-28). Treco further discloses vector embodiments wherein the transcriptional promoter can be a viral promoter (cytomegalovirus immediate early promoter), a non-viral promoter (human elongation factor-1α) or an inducible promoter (mouse metallothionein promoter-I; mMT-I) (col. 53, lines 22-30). Treco also teaches vector constructs wherein the endogenous gene encodes a transmembrane protein (e.g. receptor, col. 11, line 63); use of the recited methods for screening or producing expression products of endogenous cellular genes *in vitro* and *in vivo* (e.g. col. 4, lines 19-64 and col. 21, line 24-30); and use of linear vector constructs (e.g. col. 25, lines 46-52).

Although Treco employs targeting sequences to promote homologous recombination, use of the methods disclosed in the prior art will also result in non-homologous recombination resulting in the random activation of non-targeted genes in accordance with the methods of the claimed invention. With regard to the targeted homologous recombination technology described by Treco, Capecchi has previously reported "[r]egrettably...targeted replacement only occurs in a small fraction of the treated cells. More often, the targeting vector inserts randomly at non-matching sites or fails to integrate at all. We must therefore sort through the cells to identify those in which targeting has succeeded. Approximately one in a million treated cells has the desired replacement" (paragraph abridging pp. 56-57). Although Applicants do not explicitly recite the use of specific target sequences capable of promoting homologous recombination, there are no specific method steps to clearly distinguish between Applicants' process and that normally

occurring in any of the targeted homologous recombination schemes described by those in the prior art above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 81, 83-86, 92, and 100-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sands in view of Schmidt et al. (Mol. Cell. Biol. 10(8):4406-4411, 8/90).

Sands has been described. Sands discloses trapping genes in target cells using vectors "engineered to contain a promoter element capable of initiating transcription in virtually any cell type" (col. 8, lines 5-6) and state that other vectors can be designed using similar design considerations (col. 8, lines 23-24). Sands does not explicitly disclose methods comprising vectors wherein the promoter of the transcriptional regulatory sequence is from the cytomegalovirus immediate early promoter.

Schmidt et al. characterize the activity of the cytomegalovirus enhancer-promoter in transgenic mice and define its promoter-enhancer as "one that targets expression of a gene to the broadest possible array of tissue types...[teaching that] [g]ene constructions which contain such

pan-active elements are useful for studies designed to assess gene function in a wide range of cell types as well as in certain instances of somatic gene therapy" (p. 4406, first paragraph).

At the time the invention was made it would have been obvious to one of ordinary skill in the art to incorporate the cytomegalovirus promoter-enhancer as taught by Schmidt in the vectors of Sands, since incorporation of these regulatory elements in the vector would be predicted, with a high probability of success, to facilitate the expression of trapped genes of interest for studies to assess gene function in a wide range of cell types in accordance with the teachings of Sands concerning use of their method for gene function studies in transgenic animals. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 81, 83, 86, 87, 92, and 100-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sands in view of Bujard et al. (U.S. 5,912,411, filed 6/7/95).

Sands has been described. Sands discloses trapping genes in target cells using vectors "engineered to contain a promoter element capable of initiating transcription in virtually any cell type" (col. 8, lines 5-6) and state that other vectors can be designed using similar design considerations (col. 8, lines 23-24). Sands does not explicitly disclose methods comprising vectors wherein the promoter of the transcriptional regulatory sequence is from an inducible promoter.

Bujard teaches the usefulness of transgenic mice carrying a transgene operatively linked to an tetracycline-inducible promoter which allow the skilled artisan to control in vivo levels of transgene expression in transgenic animals and to permit stable cloning of e.g. embryonic stem cell lines transformed with toxic genes or genes limiting the ability to isolate stably transfected clones (see e.g. col. 43, lines 44-67).

At the time the invention was made it would have been obvious to one of ordinary skill in the art to incorporate the tetracycline-inducible promoter as taught by Bujard in the vectors of Sands, since incorporation of these regulatory elements in the vector would be predicted, with a high probability of success, to enhance assessment of gene function studies in transgenic animals in accordance with the teachings and goals of Sands. One would have been motivated to combine the combine the teachings of Bujard with the teachings of Sands since Bujard's teachings offer an effective way to isolate stable cell lines expressing potentially toxic products limiting complete coverage or isolation of cell lines containing trapped genes spanning the complete cellular genome. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg.*

Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 81 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 58 of copending Application Nos. 09/455,659, 09/513,575, 09/479,123, and 09/513,574 and as claiming the same invention as that of claim 85 of copending Application No. 09/276,820. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 83-88, 100, 102, and 103 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 99-104, 128, 131, and 132, respectively, of copending Application No. 09/276,820. Although the conflicting

claims are not identical, they are not patentably distinct from each other because rejected claims 83-88, 100, 102, and 103 are embraced by claims 99-104, 128, 131, and 132 of copending application 09/276,820.

Claims 81, 83-88, 92, and 100-103 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 81, 83-88, 92, and 100-103, respectively, of copending Application No. 09/479,122. Although the conflicting claims are not identical, they are not patentably distinct from each other because rejected claims 81, 83-88, 92, and 100-103 are embraced by claims 81, 83-88, 92, and 100-103 of the copending application.

Claim 100 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 88 of copending Application No. 09/481,375; claim 60 of copending Application Nos. 09/455,659 and 09/513,575; and claim 59 of copending Application Nos. 09/479,123 and 09/513,574. Although the conflicting claims are not identical, they are not patentably distinct from each other because rejected claim 100 is embraced by claim 88 of copending application 09/481,375, and because rejected claim 100 embraces the recited claims of copending applications 09/455,659, 09/513,575, 09/479,123, and 09/513,574.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

Peter Brunovskis, Ph.D.
Patent Examiner
Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER